UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/930,503 | 08/16/2001 | James L. Henry | CCT-P0011 | 1568 |

36067 7590 03/19/2007

DALINA LAW GROUP, P.C.
7910 IVANHOE AVE. #325
LA JOLLA, CA 92037

| EXAMINER | |
|---|---|
| VIVLEMORE, TRACY ANN | |
| **ART UNIT** | **PAPER NUMBER** |
| 1635 | |

| SHORTENED STATUTORY PERIOD OF RESPONSE | MAIL DATE | DELIVERY MODE |
|---|---|---|
| 3 MONTHS | 03/19/2007 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/930,503 | HENRY ET AL. | |
| | Examiner | Art Unit | |
| | Tracy Vivlemore | 1635 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *03 January 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *138-150* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *138-150* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Claim Rejections - 35 USC § 112*

Claim 150 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim is directed to treatment of "central aspects of chronic or acute pain" or treatment of "peripheral aspects of chronic or acute pain". No definition of these terms appears in the specification and they do not appear to be art-recognized terms. Therefore, the metes and bounds of this claim cannot be determined because it is unknown what conditions are encompassed by the terms "central aspects of chronic or acute pain" and "peripheral aspects of chronic or acute pain" and it is unknown what conditions are intended to be treated by this method.

Claims 138-150 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claimed invention is directed to methods of treating pathological conditions characterized by involvement of the NK-1 receptor by administration of an antisense oligonucleotide that interferes with the function or production of NK-1 receptors. The instant claims are directed to use of an oligonucleotide in order to treat a genus of pathological conditions involving the NK-1 receptor. Pathological conditions

characterized by involvement of the NK-1 receptor are disclosed in the specification as including dermatological disorders, immune disorders, autoimmune disorders, cardiovascular disorders, neuropathic disorders, vascular disorders, gut inflammation, arthritis, airway disorders, psychiatric disorders, central nervous system disorders as well as pain and inflammation of any etiology so long as involvement of the NK-1 receptor is present.

The specification describes use of antisense oligonucleotides to the NK-1 receptor to reduce pain in rats exposed to a painful stimulus. The description of a method of reducing pain does not provide description of methods for treating the numerous disorders recited in the specification. Using the generic term "immune disorders" as an example, the specification contemplates the disclosed method will be useful in treating immune disorders, but does not describe what immune disorders are characterized by involvement of the NK-1 receptor and can be treated by the instantly claimed method. The prior art does not provide a description of what immune disorders can be treated by modulation of the NK-1 receptor pathway. Without such a disclosure, the skilled artisan would not be able to recognize whether a particular immune disorder involves the NK-1 receptor pathway. The prior art also teaches that the NK-1 receptor is widely expressed in the nervous, cardiovascular and respiratory systems and the gastrointestinal tract and is implicated in pain transmission, vasodilation and smooth muscle contraction. However, in view of the teachings of the specification and the prior art that inhibition of NK-1 receptor is ineffective at treating acute conditions as outlined in the following scope of enablement rejection, the skilled artisan would not be able to recognize what pathological conditions can be treated using SEQ ID NO: 41.

In order for the written description provision of 35 USC 112, first paragraph to be satisfied, applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed. For example, MPEP 2163 states in part,

> "An adequate written description of a chemical invention also requires a precise definition, such as by structure, formula, chemical name, or physical properties, and not merely a wish or plan for obtaining the chemical invention claimed. See, e.g., *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 927, 69 USPQ2d 1886, 1894-95 (Fed. Cir. 2004) (The patent at issue claimed a method of selectively inhibiting PGHS-2 activity by administering a non-steroidal compound that selectively inhibits activity of the PGHS-2 gene product, however the patent did not disclose any compounds that can be used in the claimed methods. While there was a description of assays for screening compounds to identify those that inhibit the expression or activity of the PGHS-2 gene product, there was no disclosure of which peptides, polynucleotides, and small organic molecules selectively inhibit PGHS-2. The court held that "[w]ithout such disclosure, the claimed methods cannot be said to have been described.")."

The skilled artisan cannot envision the full genus of pathological conditions that can be treated by the instantly claimed method. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

Claims 138-150 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treatment of chronic pain or chronic inflammation by intravenous or intrathecal administration of an antisense oligonucleotide in order to interfere with production of the NK-1 receptor, does not reasonably provide enablement for treatment of all pathological conditions characterized by involvement of the NK-1 receptor, nor does it provide enablement for interfering with function of NK-1 receptors. The specification does not enable any person skilled in the art to which it pertains, or

with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The following factors as enumerated *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), are considered when making a determination that a disclosure is not enabling: the breadth of the claims, the nature of the invention, the state of the prior art, the level of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation needed to make the invention based on the content of the disclosure.

The claims are directed to methods of treating any pathological condition characterized by involvement of the NK-1 receptor using the oligonucleotide designated as SEQ ID NO: 41 to interfere with the function or production of NK-1 receptor. In specific embodiments the oligonucleotides include antisense or sense oligonucleotides or ribozymes and the oligonucleotide is administered intrathecally or intravenously.

As described in the previous rejection, the specification contemplates a wide variety of conditions including dermatological, immune or autoimmune, cardiovascular, neuropathic or airway disorders as diseases treatable by the instantly claimed methods. The working examples of the specification describe intrathecal and intravenous administration of an antisense oligonucleotide designated as SEQ ID NO: 11 that is targeted to the NK-1 receptor and is administered to rats to reduce pain resulting from exposure to a painful mechanical or chemical stimulus. These examples are not commensurate in scope with treatment of all pathological conditions characterized by involvement of the NK-1 receptor.

It is recognized by the skilled artisan that antisense oligonucleotides can affect receptor production by inhibiting expression of the gene for a receptor but do not have any effect on receptor function. Specifically, the prior art teaches (see Hua et al. Journal of Neurochemistry, of record) that use of antisense oligonucleotides to NK-1 receptors to treat acute pain found only minor effects except during co-administration of the NK-1 receptor agonist substance P. Hua et al. speculate that NK-1 receptors normally turn over at a slow rate and interfering with NK-1 receptor production may have little short-term effect on receptor numbers. Also, the specification itself acknowledges this on page 8 and teaches that the instant invention is useful for treating chronic conditions where the NK-1 receptor is experiencing high turnover but that conditions where receptor are not stimulated are unaffected:

> "...the present inventors have found that oligonucleotides, and especially antisense oligonucleotides, can be used effectively to treat chronic conditions and other pathological states without the co-administration of substance P. In such pathological states, the activation of NK-1 receptors is already high and turnover rates are commensurately rapid treatment with antisense oligonucleotides appears to reduce the number of activated receptors while not reducing the number of quiescent NK-1 receptors. Thus, the present invention targets NK-1 receptors that are active because of an existing condition to thereby ameliorate chronic pain and inflammation and disease conditions associated therewith. Receptors not chronically stimulated will be less affected, reducing side effects of treatment."

Therefore both the disclosure of the specification and what is known in the art indicates the skilled artisan would recognize that use of antisense oligonucleotides does not interfere with the function of NK-1 receptors and would not be able to treat the full range of pathological conditions that involve the NK-1 receptor. Limiting the claims to treatment of chronic pain and inflammation by inhibiting production of NK-1 receptors with an antisense oligonucleotide would be remedial.

***Response to arguments***

In the remarks filed January 3, 2007, applicants assert the new claims have been directed to subject matter (SEQ ID NO: 41) indicated by the examiner to be allowable. While it is correct that the recited sequence is free of the prior art, the scope of the new claims nevertheless encompasses undescribed and non-enabled embodiments as described in the preceding rejections.

***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has

been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
March 12, 2007